PAT NT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/009376	26.03.2004	26.03.2003

International Patent Classification (IPC) or both national classification and IPC
G01N33/68

Applicant
PRESIDENT AND FELLOWS OF HARVARD COLLEGE

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☐ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/009376

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/009376

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-33

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1-33

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

   and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

   see form 210

Re Item III.

Present claims 1-33 relate to an extremely large number of possible methods/products. In fact, the claims contain so many options, that a lack of clarity (and conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims over the whole of the claimed scope impossible. Furthermore, disclosure within the meaning of Article 5 PCT is to be found for only a very small proportion of the products/methods claimed. Consequently, the search has been carried out for those parts of the application which do appear to be clear, concise and supported, namely methods/products have been searched as recited in the examples and closely related homologous methods/products by taking into account the examples for the terms "species", "substrate" and entities" as listed in the description (p.4-8).

The applicant is also informed that the term "without substantially desalting the substrate" in claim 24 lacks clarity within the meaning of Article 6 PCT.

According to R.66.1(e) PCT, claims relating to inventions in respect of which no international search report has been established need not be the subject of international preliminary examination.

As a consequence, an opinion with respect to novelty, inventive step and industrial applicability will not be formulated for claims claims 1-33. However, a discussion of the most pertinent document cited in the international search report can be found under item V.

Re Item V.

1. Reference is made to the following documents:

   D1: SU JING ET AL: "Using mass spectrometry to characterize self-assembled monolayers presenting peptides, proteins, and carbohydrates." ANGEWANDTE CHEMIE (INTERNATIONAL ED. IN ENGLISH) 16 DEC 2002, vol. 41, no. 24, 16 December 2002 (2002-12-16), pages 4715-4718, XP002313539 ISSN: 0570-

0833

D2: NEDELKOV DOBRIN ET AL: "Design of buffer exchange surfaces and sensor chips for biosensor chip mass spectrometry" PROTEOMICS, vol. 2, no. 4, April 2002 (2002-04), pages 441-446, XP002313540 ISSN: 1615-9853

D3: WO 02/06834 A (AULT RICHE DANA ; KASSNER PAUL D (US); POINTILLISTE INC (US)) 24 January 2002 (2002-01-24)

D4: WO 2004/005918 A (MRKSICH MILAN ; SU JING (US); UNIV CHICAGO (US)) 15 January 2004 (2004-01-15)

D5: FERNANDEZ F M ET AL: "Peptide sequencing using a patchwork approach and surface-induced dissociation in sector-TOF and dual quadrupole mass spectrometers" JOURNAL OF THE AMERICAN SOCIETY FOR MASS SPECTROMETRY, ELSEVIER SCIENCE INC., NEW YORK, NY, US, vol. 14, no. 12, December 2003 (2003-12), pages 1387-1401, XP004476947 ISSN: 1044-0305

D6: TEMPLIN M F ET AL: "PROTEIN MICROARRAY TECHNOLOGY" DRUG DISCOVERY TODAY, ELSEVIER SCIENCE LTD, GB, vol. 7, no. 15, 1 August 2002 (2002-08-01), pages 815-822, XP001152984 ISSN: 1359-6446

2. D1 discloses a method for determining a species (proteins, lectins ,etc) suspected of being bound to a substrate (microarray) having an array of entities (peptide or carbohydrate ligands) bonded thereto. MALDI TOF MS is used for determination (see p. 4716, left col.). Self-assembled monolayers comprising oligo(ethylene glycol) groups are reported as highly effective at preventing nonspecific interactions with proteins (see p. 4716, left col.). The monolayer comprises maleimide groups linked to a Cys-terminated peptide (see fig.1a). Fig. 2 b of D1 shows that MALDI can be used to directly observe proteins bound to ligands immobilized on monolayers.

Re Item VI

Certain documents cited

The applicant's attention is drawn to the fact that document D3 (cited above and published on 15.1.2004, filed on 7.7.2003 with a priority dated from 5.7.2002) could become

detrimental to novelty in a later regional phase.